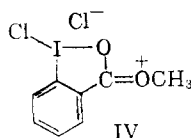


dichlorides of methyl 2- and 4-iodobenzoate were determined in nitromethane. As in acetic acid the *p*-substituted dichloride dissociated at an easily measurable rate, but its *o*-isomer reached equilibrium with its components too rapidly for kinetic measurements to be made. The methoxyl, like the chlorine of the *o*-COCl group, should have an unfavorable inductive effect on the nucleophilic character of the *o*-COOCH<sub>3</sub> group. However this inductive influence may be over-shadowed by the contribution of methoxyl to resonance stabilization of the activated complex (*cf.* structure IV). It is, of course, possible that the methoxyl oxygen itself



may be the nucleophilic center for coordination of *o*-COOCH<sub>3</sub> with the iodine atom.

No clear definition of the structural requirements of *o*-substituents for nucleophilic participation in the iodobenzene dichloride equilibration process can as yet be made.<sup>17</sup> Certainly the activation energy required for dissociation must be substantially lowered by those substituents which are effective participants. The activation energy for dichloride formation, in these cases, should also be reduced. As may be expected the *k*<sub>2</sub>-values (equation 1), as well as the *k*<sub>1</sub>-values, for equilibration processes in which the *ortho* effect is observed are (in cases where data are available) substantially larger than those for reactions of the corresponding

(17) From an inspection of molecular models it appears that the *o*-COOCH<sub>3</sub> and *o*-CONHC<sub>6</sub>H<sub>5</sub> groups are ideally constituted structurally for effective participation (see structures III and IV). It is noteworthy that of all the *o*-substituted dichlorides which have been investigated so far those of methyl 2-iodobenzoate and 2'-iodobenzanilide are the most reactive.

*p*-isomers. However the *ortho* effects are more noticeably manifested in *k*<sub>1</sub> than *k*<sub>2</sub>-values. Unfortunately the reactions which are markedly influenced by neighboring groups are sufficiently fast so that it is experimentally impracticable to obtain thermodynamic data for activation processes by the methods of this investigation. A comparison of energies and entropies of activation for the highly reactive *o*-substituted dichlorides and their *p*-isomers would be of considerable value in interpreting the nature of the *o*-substituent effect.

The equilibrium constants at 25.0 and 45.2°, reported in Table II, for the dichlorides of 2-iodoacetanilide and 2-iodobenzyl alcohol were used to calculate the heats and entropies of dissociation. These constants and those for the dichlorides of 2- and 4-iodophenyl benzoates, as well as the entropies and energies of activation for dissociation of the benzoate derivatives, are listed in Table III.

TABLE III  
THERMODYNAMIC CONSTANTS FOR DISSOCIATION OF SUBSTITUTED IODOBENZENE DICHLORIDES IN ACETIC ACID

| Substituent   | $\Delta H^\circ$ ,<br>kcal./mole | $\Delta S^\circ$ ,<br>e.u. | $E_1$ ,<br>kcal./mole | $-\Delta S_1^\ddagger$ ,<br>e.u. |
|---|----------------------------------|----------------------------|-----------------------|----------------------------------|
| $\text{O}$<br>2-NHCCH <sub>3</sub>                            | 8.2 ± 0.7                        | 19.4 ± 2.3                 | .....                 | .....                            |
| 2-CH <sub>2</sub> OH  | 8.0 ± 0.4                        | 15.4 ± 1.3                 | .....                 | .....                            |
| 4-OCC <sub>6</sub> H <sub>5</sub>                             | 8.8 ± 0.2                        | 17.9 ± 0.7                 | 18.8 ± 0.3            | 14.8 ± 1.0                       |
| $\text{O}$<br>2-OCC <sub>6</sub> H <sub>5</sub><br>$\text{O}$ | 9.3 ± 1.3                        | 23.1 ± 4.4                 | 18.5 ± 0.4            | 13.2 ± 1.3                       |

In general the thermodynamic constants resemble those found for reactions of other dichlorides in acetic acid, and they are unrevealing so far as the present discussion is concerned.

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DAVIS, CALIF.

[CONTRIBUTION FROM MONSANTO CHEMICAL CO., PLASTICS DIVISION RESEARCH DEPARTMENT]

## The Catalytic Effect of Water on the Cyanoethylation of *t*-Carbinamines

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Water and other compounds possessing a labile hydrogen attached to an atom having a pair of electrons available for complex formation are active catalysts for the cyanoethylation of *t*-carbinamines. A mechanism is proposed which involves proton transfer by the "catalyst" as the step terminating the reaction. Steric factors of reactants and "catalysts" as well as solubility characteristics are considered.

### Introduction

The cyanoethylation reaction (Michael addition of active hydrogen compounds to the double bond of acrylonitrile) has been widely studied and mechanisms for the reaction with alcohols, amines and ketones have been postulated.<sup>1-5</sup>

(1) H. Bruson, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 84.

(2) Y. Ogato, M. Okano, Y. Furuya and I. Tabushi, *THIS JOURNAL*, **78**, 5426 (1956).

(3) G. R. Zellars and Robert Levine, *J. Org. Chem.*, **13**, 911 (1948).

(4) S. A. Heiniger, *ibid.*, **22**, 1213 (1957).

(5) U. Hofmann and B. Jacobi, U. S. Patent 1,992,615 (to I. G. Farbenindustrie).

Recent work has described yield improvements in cyanoethylation of *t*-carbinamines of highly branched structure by using dilute aqueous acidic catalysts.<sup>8</sup> In this fashion, the yield of the cyanoethylated derivative of *t*-butylamine was increased from about 5 to 89% and the yield, using 1,1,3,3-tetramethylbutylamine, was raised from 0 to 83%. It has now been found that these other supposed

(6) F. C. Whitmore, H. S. Mosher, R. R. Adams, R. B. Taylor, E. C. Chapin, C. Weisel and W. Yanko, *THIS JOURNAL*, **66**, 725 (1944).

(7) D. S. Tarbell, N. Shakespeare, C. J. Claus and J. F. Burnett, *ibid.*, **68**, 1217 (1946).

(8) L. S. Luskin, M. J. Culver, G. E. Gantert, W. F. Craig and R. S. Cook, *ibid.*, **78**, 4043 (1956).

catalysts are not needed for these yield increases because water alone catalyzes the cyanoethylation of *t*-carbinamines.

In our study of the cyanoethylation of sterically hindered amines, especially *t*-carbinamines (*t*-alkyl-primary amines), water or other labile hydrogen-containing compounds have been found to exert a remarkable effect on the reaction. Under substantially anhydrous conditions, hindered amines undergo cyanoethylation much more difficultly than do unhindered amines. For example, *n*-butylamine is readily cyanoethylated in 85–95% yield, *t*-butylamine is cyanoethylated only in 4.8–5.6% yield, and 1,1,3,3-tetramethylbutylamine gives no yield. In each case of hindered amine cyanoethylation studied, only the monocyanoethyl derivative was produced; no dicyanoethylated products were formed.

### Experimental

**Acrylonitrile.**—Acrylonitrile used was Monsanto product acrylonitrile dried over Drierite to a water content of less than 0.1% as determined by a Karl Fischer titration.

**Amines.**—The *t*-carbinamines used in this study were all prepared by the reaction of HCN with the corresponding olefin in the presence of sulfuric acid.<sup>9</sup> The olefins used were isobutylene, diisobutylene and propylene trimer. The amine prepared from propylene trimer is a mixture of structural isomers, but all of these amines contain the *t*-carbinamine structure. The amines were also dried over Drierite or sodium to a water content of less than 0.1%.

**General Cyanoethylation Procedure.**—The general procedure used in cyanoethylation of amines in this work is illustrated using *t*-butylamine. This method was chosen as the standard because of its simplicity and convenience. For the other amines studied, only actual weights of reactants were varied.

A mixture of *t*-butylamine (73.0 g., 1 mole) and water (7.3 g., 0.4 mole) was stirred and heated under reflux (45° when *t*-butylamine was used; 78° when other amines were used) while acrylonitrile (53 g., 1 mole) was added dropwise over a period of 30 min. Stirring and heating were continued for an additional hour. The water, unreacted *t*-butylamine and acrylonitrile were then rapidly distilled overhead and the residue was distilled under vacuum to give  $\beta$ -(*N*-*t*-butylamino)-propionitrile (113.4 g., 0.9 mole) in 90% yield. The product boiled at 50–52° (1 mm.).

The products were isolated by fractional distillation and identified by infrared spectroscopy; all products, even though mixtures of structural isomers when the nonylamine derived from propylene trimer was used as the amine, were determined to be the monocyanoethyl derivatives.  $\beta$ -(*t*-Nonylamino)-propionitrile, a new compound, boils at 109–111° (1.5 mm.).

**Reversal of Cyanoethylation.**—Samples of  $\beta$ -(*N*-*n*-butylamino)-propionitrile and  $\beta$ -(*N*-*t*-butylamino)-propionitrile were heated by means of an oil-bath both in the absence and presence of water. Any distillate or evolved vapors were neutralized with sulfuric acid in a trap attached to the system and the amount of amine trapped was determined by back-titration of the acid. The systems were flushed into the acid traps with a stream of air to ensure full recovery of regenerated amine. The reversal reactions were run at 110–120°, a temperature at which either amine (*t*-butylamine, b.p. 45° or *n*-butylamine, b.p. 77°) should distil readily from the system. In these runs it was found that no free amine was liberated when the 3-*N*-alkylaminopropionitriles were heated alone. In the presence of water, however, 6% of the available *n*-butylamine was found after 4 hours heating and 10% of the available *t*-butylamine was found after 6 hours heating.

### Discussion

Two parallel series of runs were made in which *t*-butylamine, 1,1,3,3-tetramethylbutylamine and *t*-nonylamine were cyanoethylated according to the above procedure. In one series the dry reactants

were used while in the second series, water in varying amounts was added to study its effect. Results of these runs are given in Table I. The yields were always substantially zero in the anhydrous runs and ranged from 95.5% for *t*-butylamine to 27% for nonylamine when water was added.

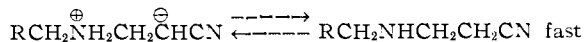
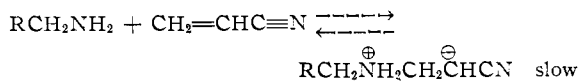
TABLE I  
EFFECT OF WATER ON CYANOETHYLATION OF *t*-CARBINAMINES

|                               | Moles amine per mole AN | Catalyst, <sup>a</sup> % water added | Conversion, % |
|-------------------------------|-------------------------|--------------------------------------|---------------|
| <i>t</i> -Butylamine          | 1.5                     | 0                                    | 4.8           |
| <i>t</i> -Butylamine          | 1.5                     | 3.4                                  | 77.1          |
| <i>t</i> -Butylamine          | 1.5                     | 10.0                                 | 95.5          |
| <i>t</i> -Butylamine          | 1.0                     | 10.0                                 | 90.0          |
| 1,1,3,3-Tetramethylbutylamine | 1.0                     | 0                                    | 0             |
| <i>t</i> -Nonylamine          | 1.0                     | 10                                   | 71.5          |
| <i>t</i> -Nonylamine          | 1.0                     | 0                                    | 0             |
| <i>t</i> -Nonylamine          | 1.0                     | 10                                   | 26.8          |

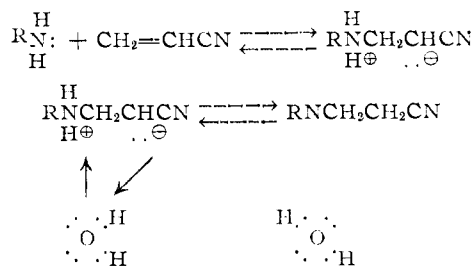
<sup>a</sup> The amount of water added is given as weight per cent. based on the weight of amine used.

The solubility of water in the amines used in this study decreases rapidly as the molecular weight of the amine increases. While this lack of solubility in the higher amines removes water from its role in this reaction, resulting in lower conversions, the addition of a component which brings about homogeneity of the reacting system, but is otherwise inert in the system, restores the catalytic effect of the water. The results of runs showing these effects are given in Table II. That *N,N*-dimethylformamide is non-catalytic itself in the cyanoethylation reaction is shown by its failure to catalyze the cyanoethylation of 1,1,3,3-tetramethylbutylamine.

**Mechanism.**—The mechanism of the cyanoethylation reaction has been postulated as attack by an anion or available electron pair at the terminal carbon atom of the acrylonitrile followed by loss and gain of protons as needed to complete the reaction.<sup>1–3</sup> Thus, in the case of amines the mechanism has been postulated as



It is now believed that the concluding step, previously considered the fast step, may, because of steric factors, be the rate-determining step and that the effect of water as reported here is in the role of a proton transfer agent effecting completion of the reaction



For a compound to act as proton transfer agent under these conditions, it must have an unshared

(9) J. J. Ritter and P. P. Minieri, THIS JOURNAL, 70, 4045 (1948).

TABLE II

EFFECT OF SOLUBILIZING AGENTS ON WATER-CATALYZED CYANOETHYLATION OF *t*-CARBINAMINES

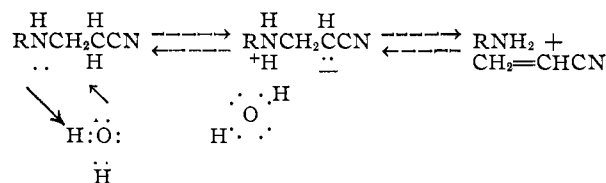
|                               | Mole amine per mole AN fed | Catalyst <sup>a</sup> | Solubilizer <sup>a</sup>         | Conversion of amine to <i>N</i> - $\beta$ -cyanoethyl product, % |
|-------------------------------|----------------------------|-----------------------|----------------------------------|--|
| <i>t</i> -Nonylamine          | 1.0                        | None                  | None                             | 0  |
| <i>t</i> -Nonylamine          | 1.0                        | 10% water             | None                             | 26.8   |
| <i>t</i> -Nonylamine          | 1.0                        | 10% water             | 10% <i>N,N</i> -DMF <sup>b</sup> | 41.0   |
| <i>t</i> -Nonylamine          | 1.0                        | 10% water             | 20% <i>N,N</i> -DMF <sup>b</sup> | 66.5   |
| 1,1,3,3-Tetramethylbutylamine | 1.0                        | 0                     | 10% <i>N,N</i> -DMF <sup>b</sup> | 0  |

<sup>a</sup> The amounts of water and solubilizer added are given as weight percentages based on the weight of amine used.  
<sup>b</sup> *N,N*-DMF = *N,N*-dimethylformamide.

pair of electrons with a labile hydrogen atom on the same atom which contains the unshared pair and the geometry of the proton transfer agent must allow it to physically fit the cyanoethylation intermediate. Thus, unhindered amines, alcohols, amides, thiols and the like should be effective in such a role. In the cyanoethylation of unhindered amines, excess of unreacted amine itself can satisfactorily act as transfer agent leading to high yields of product. In the case of highly hindered amines, such as the *t*-carbinamines, the steric hindrance around the amine group prevents it from approaching the similarly hindered cyanoethylation intermediate to allow completion of the reaction. These effects become obvious only in essentially anhydrous reaction systems.

The amounts of water usually found in the reagents used in these reactions are enough to promote cyanoethylation. Many cyanoethylation reactions previously reported have undoubtedly have been greatly influenced by the presence of small amounts of water in the reagents.<sup>7,8</sup>

If the proposed role of water in this system is correct, a similar effect should be found in the reversal of cyanoethylation. When certain cyanoethylated products are heated in the presence of the catalyst used for reaction, acrylonitrile and the originally cyanoethylated compound can be distilled from the reaction mixture. We have found that pure 3-*N*-alkylaminopropionitriles do not revert readily to acrylonitrile and amine when heated to 120°. Considering the fact that proton transfer would again be necessary to effect reversal of the reaction



it would be expected that pure anhydrous amine cyanoethylation products would not readily revert to acrylonitrile and amine.

In order to evaluate this hypothesis experimentally, the reversal of amine cyanoethylation was studied. It was found that reversal of reaction did not occur when the anhydrous 3-alkylaminopropionitriles were heated, but that when heated in the

TABLE III

EFFECT OF ACTIVE HYDROGEN-CONTAINING COMPOUNDS ON CYANOETHYLATION OF *t*-BUTYLAMINE

| Moles amine per mole AN fed | Catalyst <sup>a</sup>                                  | Mole of catalyst per mole of amine | Conversion of amine to <i>N</i> - $\beta$ -cyanoethyl prod., % |
|-----------------------------|--|------------------------------------|--|
| 1.5                         | None   |                                    | 0  |
| 1.0                         | 10% HOH  |                                    | 90.0   |
| 1.0                         | 10% CH <sub>3</sub> OH                                 |                                    | 57.8   |
| 1.0                         | 10% CH <sub>3</sub> CH <sub>2</sub> OH                 |                                    | 42.8   |
| 1.0                         | 10% CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OH | 0.12                               | 38.7   |
| 1.0                         | 10% CH <sub>3</sub> CHOHCH <sub>3</sub>                | .12                                | 28.7   |
| 1.0                         | 10% (CH <sub>3</sub> ) <sub>2</sub> COH                | .10                                | 17.5   |
| 1.0                         | 12% (CH <sub>3</sub> ) <sub>2</sub> COH                | .12                                | 20.6   |
| 1.0                         | 10% CH <sub>3</sub> COOH                               |                                    | 29.3   |
| 1.0                         | 20% HCONH <sub>2</sub>                                 |                                    | 92.8   |

<sup>a</sup> The amount of catalyst used is given as weight per cent. based on the weight of amine used.

presence of water, appreciable reversal of cyanoethylation to give free amines did occur.

A consideration of all these effects led to the conclusion that certain other compounds containing the required structure, *i.e.*, a labile hydrogen atom attached to an atom which also has a free pair of electrons, should act as catalysts for cyanoethylation of sterically hindered amines.

Table III lists the results of evaluation of a number of compounds (alcohols, acids and amides) as catalysts. For these evaluations the "standard" procedure as given under the Experimental section was used with variations in reactant ratios and catalyst materials added as shown in the table.

It is of interest to note that the effectiveness of alcohols as catalysts decreases as the molecular complexity of the alcohol increases. That this decrease is not merely a concentration effect is shown by runs in which equimolar amounts of *n*-propyl-, isopropyl- and *t*-butyl alcohols were used as catalysts (see Table III). According to the proposed mechanism, this effect is the result of increasing difficulty in the alcohol approaching the intermediate to act as a proton transfer agent to complete the reaction.

The data presented here do not eliminate an effect due purely to differences in the nature of the solvent, *i.e.*, polarity, dielectric strength, etc. However, comparison of the dielectric constants of compounds employed as catalysts fails to disclose any trend which might be affected by dielectric character. No other characteristics of the materials used as catalysts have been found to be directly relatable to their catalytic activity. Thus, the proposed mechanism fits the facts more closely than any proposal based purely on solvent effects.

The use of tritiated water or alcohols as the catalyst was considered as a means of establishing the mechanism, but had to be eliminated because of the rapid equilibration between catalyst and amine being cyanoethylated.

**Acknowledgment.**—We wish to acknowledge the assistance of Professor R. B. Turner and Dr. G. A. Mortimer in developing the proposed mechanism.

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